#### PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \* \* \* SESSION RESUMED IN FILE 'STNGUIDE' AT 18:15:55 ON 22 FEB 2008 FILE 'STNGUIDE' ENTERED AT 18:15:55 ON 22 FEB 2008 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST

=> file registry
COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY

SESSION

FULL ESTIMATED COST 0.06 30.95

FILE 'REGISTRY' ENTERED AT 18:16:03 ON 22 FEB 2008
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STRUCTURE FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9 DICTIONARY FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

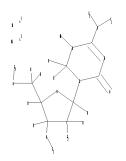
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

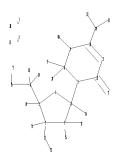
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http://www.cas.org/support/stngen/stndoc/properties.html

=> Uploading C:\Program Files\Stnexp\Queries\10670915generic.str





```
chain nodes :
6  13  14  15  16  17  18  19  20  22  23  26  27  28  32  33  35  37  38  39  40

ring nodes :
1  2  3  4  5  7  8  9  10  11  12
chain bonds :
1-18  1-27  2-6  2-19  4-7  4-16  5-17  5-26  6-35  6-38  6-39  8-15  8-20  9-40
10-14  12-13  14-22  14-23  27-32  35-37
ring bonds :
1-2  1-5  2-3  3-4  4-5  7-8  7-12  8-9  9-10  10-11  11-12
exact/norm bonds :
1-2  1-5  1-27  2-3  3-4  4-5  4-7  5-26  6-35  7-8  7-12  8-9  9-10  9-40  10-11
10-14  11-12  12-13  14-22  14-23  27-32  35-37
exact bonds :
```

1-18 2-6 2-19 4-16 5-17 6-38 6-39 8-15 8-20

G1:C,H G2:H,OH,MeO G3:H, [\*1] G4:H,P,[\*2] Connectivity: 28:0 E exact RC ring/chain 40:0 E exact RC ring/chain Match level: 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 22:CLASS 23:CLASS 26:CLASS 27:CLASS 28:CLASS 32:CLASS 33:CLASS 35:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS Generic attributes : 28: Saturation : Saturated Number of Carbon Atoms : less than 7 33: : Saturated Number of Carbon Atoms : less than 7 40: Saturation : Saturated Number of Carbon Atoms : less than 7 L11 STRUCTURE UPLOADED => s 111 SAMPLE SEARCH INITIATED 18:16:24 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 1725 TO ITERATE 100.0% PROCESSED 1725 ITERATIONS 0 ANSWERS SEARCH TIME: 00.00.01 FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\* BATCH \*\*COMPLETE\*\* PROJECTED ITERATIONS: 32009 TO 36991 0 TO PROJECTED ANSWERS: 0 SEA SSS SAM L11 L12 => d 111

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \* Structure attributes must be viewed using STN Express query preparation.

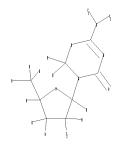
=>

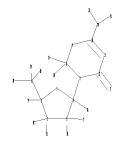
L11

L11 HAS NO ANSWERS

STR

Uploading C:\Program Files\Stnexp\Queries\10670915broad.str





```
chain nodes :
6  13  14  15  16  17  18  19  20  22  23  26  27  28  29  30
ring nodes :
1  2  3  4  5  7  8  9  10  11  12
chain bonds :
1-18  1-27  2-6  2-19  4-7  4-16  5-17  5-26  6-28  6-29  6-30  8-15  8-20  10-14
12-13  14-22  14-23
ring bonds :
1-2  1-5  2-3  3-4  4-5  7-8  7-12  8-9  9-10  10-11  11-12
exact/norm bonds :
1-2  1-5  1-27  2-3  3-4  4-5  4-7  5-26  6-28  7-8  7-12  8-9  9-10  10-11  10-14
11-12  12-13  14-22  14-23
exact bonds :
1-18  2-6  2-19  4-16  5-17  6-29  6-30  8-15  8-20
```

G1:C,H

G2:H,O

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS

22:CLASS 23:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS

#### L13 STRUCTURE UPLOADED

=> s 113

SAMPLE SEARCH INITIATED 18:17:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1725 TO ITERATE

100.0% PROCESSED 1725 ITERATIONS 1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 32009 TO 36991 PROJECTED ANSWERS: 1 TO 80

L14 1 SEA SSS SAM L13

=> d 114 scan

L14 1 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN 1,3,5-Triazine-1(2H)-sulfonic acid, 6-amino-3,4-dihydro-4-oxo-3- $\beta$ -D-ribofuranosyl-

MF C8 H14 N4 O8 S

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> s 113 sss full

FULL SEARCH INITIATED 18:18:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 35390 TO ITERATE

100.0% PROCESSED 35390 ITERATIONS

SEARCH TIME: 00.00.01

L15 45 SEA SSS FUL L13

=> d 115 scan

L15 45 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN

IN 1,3,5-Triazin-2(1H)-one, 4-amino-1-[2-deoxy-3,5-bis-O-(4-methylbenzoyl)- $\beta$ -D-erythro-pentofuranosyl]-3,6-dihydro- (9CI)

45 ANSWERS

MF C24 H26 N4 O6

CI COM

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L15 45 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN IN 1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy- $\beta$ -D-erythro-pentofuranosyl)-3,6-dihydro-, compd. with 4-amino-1-(2-deoxy- $\beta$ -D-erythro-pentofuranosyl)-1,3,5-triazin-2(1H)-one (1:1) (9CI) MF C8 H14 N4 O4 . C8 H12 N4 O4

CM 1

Absolute stereochemistry.

CM 2

Absolute stereochemistry.

L15 45 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN IN Carbamic acid, [5-(2-deoxy- $\beta$ -D-erythro-pentofuranosyl)-1,4,5,6-tetrahydro-4-oxo-1,3,5-triazin-2-yl]-, pentyl ester (9CI) MF C14 H24 N4 O6

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus
COST IN U.S. DOLLARS

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
179.74
210.69

FILE 'CAPLUS' ENTERED AT 18:18:18 ON 22 FEB 2008
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=> s 115

L16 93 L15

=> file registry
COST IN U.S. DOLLARS

FULL ESTIMATED COST ENTRY SESSION 0.48 211.17

SINCE FILE

TOTAL

FILE 'REGISTRY' ENTERED AT 18:18:29 ON 22 FEB 2008
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=> s 111 sub=115 ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):full FULL SUBSET SEARCH INITIATED 18:18:52 FILE 'REGISTRY' FULL SUBSET SCREEN SEARCH COMPLETED -45 TO ITERATE

100.0% PROCESSED 45 ITERATIONS 0 ANSWERS SEARCH TIME: 00.00.01

L17 0 SEA SUB=L15 SSS FUL L11

=> s 111 sss full FULL SEARCH INITIATED 18:18:59 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 35390 TO ITERATE

100.0% PROCESSED 35390 ITERATIONS 0 ANSWERS SEARCH TIME: 00.00.03

0 SEA SSS FUL L11 T.18

=> file caplus COST IN U.S. DOLLARS

SINCE FILE TOTAL SESSION ENTRY FULL ESTIMATED COST 220.46 431.63

FILE 'CAPLUS' ENTERED AT 18:19:08 ON 22 FEB 2008 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

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=> s 116 and (PY<2003 or AY<2003 or PRY<2003)

22928694 PY<2003

4477361 AY<2003

3952568 PRY<2003

L19 74 L16 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> loghold

LOGHOLD IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> log hold

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 7.32 438.95

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 18:20:30 ON 22 FEB 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \* \* SESSION RESUMED IN FILE 'CAPLUS' AT 18:21:39 ON 22 FEB 2008 FILE 'CAPLUS' ENTERED AT 18:21:39 ON 22 FEB 2008 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)f

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
7.32
438.95

=> file registry

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 7.32 438.95

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STRUCTURE FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9 DICTIONARY FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

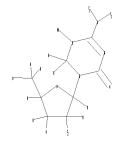
Please note that search-term pricing does apply when conducting SmartSELECT searches.

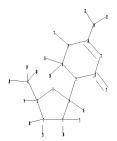
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>

Uploading C:\Program Files\Stnexp\Queries\10670915step2.str





chain nodes :
6 13 14 15 16 17 18 19 20 22 23 26 27 28 29 30 31
ring nodes :
1 2 3 4 5 7 8 9 10 11 12
chain bonds :
1-18 1-27 2-6 2-19 4-7 4-16 5-17 5-26 6-28 6-29 6-30 8-15 8-20 9-31
10-14 12-13 14-22 14-23
ring bonds :
1-2 1-5 2-3 3-4 4-5 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-5 1-27 2-3 3-4 4-5 4-7 5-26 6-28 7-8 7-12 8-9 9-10 9-31 10-11
10-14 11-12 12-13 14-22 14-23
exact bonds :
1-18 2-6 2-19 4-16 5-17 6-29 6-30 8-15 8-20

G1:C,H

G2:H,O

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 20:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS Generic attributes: 31:

Saturation : Saturated Number of Carbon Atoms : less than 7

#### L20 STRUCTURE UPLOADED

=> s 120 sub=115 ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):full FULL SUBSET SEARCH INITIATED 18:22:02 FILE 'REGISTRY' FULL SUBSET SCREEN SEARCH COMPLETED - 45 TO ITERATE

100.0% PROCESSED 45 ITERATIONS 2 ANSWERS SEARCH TIME: 00.00.01

L21 2 SEA SUB=L15 SSS FUL L20

=> d 121 scan

L21 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN IN 1,3,5-Triazin-2(1H)-one, 4-amino-5,6-dihydro-5-methyl-1- $\beta$ -D-ribofuranosyl-MF C9 H16 N4 O5

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L21 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy-β-D-erythro-pentofuranosyl)-5,6-dihydro-5-methylMF C9 H16 N4 O4

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> fiel caplus
FIEL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not a

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> s 121

SAMPLE SEARCH INITIATED 18:22:17 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1725 TO ITERATE

100.0% PROCESSED 1725 ITERATIONS SEARCH TIME: 00.00.01

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 32009 TO 36991 PROJECTED ANSWERS: 0 TO

L22 0 SEA SSS SAM L20

=> file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 42.56 481.51

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=> s 121

L23 2 L21

=> d 123 1-2 ti abs bib

L23 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN ΤI Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof

GT

- The invention discloses a genus of nucleoside or nucleotide analogs I, AΒ wherein Y = C, CH, N; Z = C, CH, B; R1 = H, acyl, OR9, SR9, substituted sec-amine, NHNH2, O, :NR9; R9 is H, alkyl, acyl, heteroalkyl, aryl; R2 = absent, H, acyl, alkyl, halogen, O, substituted o, substituted N; R3 = H, acyl, alkyl, substituted sec-amine, substituted oxime, substituted S, O, substituted O; R4, R4a = H, halo, OMe, OH; R5, R6 = H, OR14 (R14 = H, (un) substituted alkyl); R7, R8 = absent, H, acyl, alkyl; R1R8 together with the atom to which they are attached form cycloalkyl, heterocycloalkyl; were prepared for use as antiviral agents. In another aspect, the nucleoside and nucleotide analogs I are used to treat a viral disease by administering a therapeutically effective amount of I to patient with a viral disease which is caused by an RNA virus, a DNA virus, a retrovirus, or HIV. Thus, 2'-deoxy-5,6-dihydro-5-azacytidine palmitate was prepared and was tested in vitro and in rats and dogs as antiviral agent.
- AN 2007:993619 CAPLUS <<LOGINID::20080222>>
- DN 147:315014
- TI Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof
- IN Daifuku, Richard; Gall, Alexander; Sergueev, Dmitri
- PA Koronis Pharmaceuticals, Inc., USA
- SO U.S. Pat. Appl. Publ., 55pp., Cont.-in-part of U.S. Ser. No. 670,915. CODEN: USXXCO
- DT Patent
- LA English

FAN.CNT 2

	0111 1				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	US 2007207973	A1	20070906	US 2006-616693	20061227
	US 2004127436	A1	20040701	US 2003-670915	20030924
	US 2007142310	A1	20070621	US 2007-671964	20070206
PRAI	US 2002-413337P	Р	20020924		
	US 2003-670915	A2	20030924		
OS	MARPAT 147:315014				

- L23 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof GI

```
The invention discloses a genus of nucleoside or nucleotide analogs I
AΒ
    [Y=C, CH, N; Z=C,CH,B; R1=H, acyl, NHNH2, etc; R2=absent, H, acyl, etc;
    R3=H, acyl, (un)substituted alkyl, etc.; R4, R4a=H, halo, OMe, OH; R5,
    R6=H, OR14 (R14= H, (un)substituted alkyl, etc.;) R7,R8=absent, H, acyl,
    etc.] for use as antiviral agents. In a first aspect, there is provided a
    compound according to Formula I as shown. In another aspect, the nucleoside
    and nucleotide analogs according to Formula I are used to treat a viral
    disease by administrating a therapeutically effective amount of a compound of
    Formula I to patient with a viral disease which is caused by an RNA virus,
    a DNA virus, a retrovirus, or HIV. Preparation of selected analogs is
    described.
    2004:290464 CAPLUS <<LOGINID::20080222>>
ΑN
DN
    140:297477
ΤI
    Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide
    analogs, and preparation thereof
    Daifuku, Richard; Gall, Alexander; Sergueev, Dmitri
IN
    Koronis Pharmaceuticals, Incorporated, USA
PΑ
    PCT Int. Appl., 108 pp.
SO
    CODEN: PIXXD2
DT
    Patent
LA
    English
FAN.CNT 2
                       KIND
    PATENT NO.
                               DATE
                                          APPLICATION NO.
                               _____
                                           _____
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    WO 2004028454 A2
                                          WO 2003-US30200
                               20040408
                                                                  20030924
PΙ
    WO 2004028454
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            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
            GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
            LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
            OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
            TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                                          EP 2003-770420
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            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
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PRAI US 2002-413337P
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    WO 2003-US30200
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                              20030924
    MARPAT 140:297477
OS
=> d his
     (FILE 'HOME' ENTERED AT 17:16:41 ON 22 FEB 2008)
    FILE 'HCAPLUS' ENTERED AT 17:17:47 ON 22 FEB 2008
           3474 S PNEUMOCOCCUS OR (PNEUMONIDAE)
L1
          14243 S (TYPE 5) OR (TYPE V)
L2
L3
           114 S QUINOVOSAMINE
             0 S L1 AND L2 AND L3
L4
    FILE 'STNGUIDE' ENTERED AT 17:17:50 ON 22 FEB 2008
    FILE 'HCAPLUS' ENTERED AT 17:18:43 ON 22 FEB 2008
L5
         31118 S PNEUMOCOCCUS OR (PNEUMONIAE)
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L6		0 S L5 AND L2 AND L3	
	FILE	'STNGUIDE' ENTERED AT 17:18:46 ON 22 FEB 2008	
L7	FILE	'HCAPLUS' ENTERED AT 17:18:58 ON 22 FEB 2008 3474 S L1 AND L5	
	FILE	'STNGUIDE' ENTERED AT 17:18:59 ON 22 FEB 2008	
L8	FILE	'HCAPLUS' ENTERED AT 17:19:19 ON 22 FEB 2008 38 S L2 AND L5	
	FILE	'STNGUIDE' ENTERED AT 17:19:20 ON 22 FEB 2008	
L9	FILE	'HCAPLUS' ENTERED AT 17:19:36 ON 22 FEB 2008 31 S L8 AND (PY<2003 OR AY<2003 OR PRY<2003)	
	FILE	'STNGUIDE' ENTERED AT 17:19:40 ON 22 FEB 2008	
	FILE	'HCAPLUS' ENTERED AT 17:19:53 ON 22 FEB 2008	
	FILE	'STNGUIDE' ENTERED AT 17:19:54 ON 22 FEB 2008	
L10		'HCAPLUS' ENTERED AT 17:20:50 ON 22 FEB 2008 0 S L3 AND L5	
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L11 L12 L13 L14 L15		'REGISTRY' ENTERED AT 18:16:03 ON 22 FEB 2008 STRUCTURE UPLOADED 0 S L11 STRUCTURE UPLOADED 1 S L13 45 S L13 SSS FULL	
L16	FILE	'CAPLUS' ENTERED AT 18:18:18 ON 22 FEB 2008 93 S L15	
L17 L18		'REGISTRY' ENTERED AT 18:18:29 ON 22 FEB 2008 0 S L11 SUB=L15 FULL 0 S L11 SSS FULL	
L19	FILE	'CAPLUS' ENTERED AT 18:19:08 ON 22 FEB 2008 74 S L16 AND (PY<2003 OR AY<2003 OR PRY<2003)	
L20 L21 L22		'REGISTRY' ENTERED AT 18:21:45 ON 22 FEB 2008 STRUCTURE UPLOADED 2 S L20 SUB=L15 FULL 0 S L21	
L23	FILE	'CAPLUS' ENTERED AT 18:22:23 ON 22 FEB 2008 2 S L21	
	og hol	ld .S. DOLLARS SINCE FILE TOTAL ENTRY SESSION	
FULL	ESTI	MATED COST 6.30 487.81	
		AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION	
CA S	UBSCR.	IBER PRICE -1.60 -1.60	J

## SESSION WILL BE HELD FOR 120 MINUTES STN INTERNATIONAL SESSION SUSPENDED AT 18:22:38 ON 22 FEB 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSPTAEXO1623

### PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \* \* SESSION RESUMED IN FILE 'CAPLUS' AT 18:23:34 ON 22 FEB 2008 FILE 'CAPLUS' ENTERED AT 18:23:34 ON 22 FEB 2008 COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 6.30 487.81 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -1.60-1.60

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93 L15

981638 THU/RL

L24

35 L15/THU (L15 (L) THU/RL)

=> s 124 and (PY<2003 or AY<2003 or PRY<2003)

22928694 PY<2003

4477361 AY<2003

3952568 PRY<2003

L25 23 L24 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d 125 1-23 ti abs bib hitstr

L25 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof

GΙ

AB The invention discloses a genus of nucleoside or nucleotide analogs I, wherein Y = C, CH, N; Z = C, CH, B; R1 = H, acyl, OR9, SR9, substituted sec-amine, NHNH2, O, :NR9; R9 is H, alkyl, acyl, heteroalkyl, aryl; R2 = absent, H, acyl, alkyl, halogen, O, substituted o, substituted N; R3 = H, acyl, alkyl, substituted sec-amine, substituted oxime, substituted S, O, substituted O; R4, R4a = H, halo, OMe, OH; R5, R6 = H, OR14 (R14 = H, (un) substituted alkyl); R7, R8 = absent, H, acyl, alkyl; R1R8 together with the atom to which they are attached form cycloalkyl, heterocycloalkyl; were prepared for use as antiviral agents. In another aspect, the nucleoside and nucleotide analogs I are used to treat a viral disease by administering a therapeutically effective amount of I to patient with a viral disease which is caused by an RNA virus, a DNA virus, a retrovirus, or HIV. Thus, 2'-deoxy-5,6-dihydro-5-azacytidine palmitate was prepared and was tested in vitro and in rats and dogs as antiviral agent.

AN 2007:993619 CAPLUS <<LOGINID::20080222>>

DN 147:315014

TI Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof

IN Daifuku, Richard; Gall, Alexander; Sergueev, Dmitri

PA Koronis Pharmaceuticals, Inc., USA

SO U.S. Pat. Appl. Publ., 55pp., Cont.-in-part of U.S. Ser. No. 670,915. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	US 2007207973	A1	20070906	US 2006-616693	20061227 <
	US 2004127436	A1	20040701	US 2003-670915	20030924 <
	US 2007142310	A1	20070621	US 2007-671964	20070206 <
PRAI	US 2002-413337P	P	20020924	<	
	US 2003-670915	A2	20030924		
OS	MARPAT 147:315014				

OS MARPAI 14/:3150

IT 114522-16-6P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(treatment of viral diseases 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof)

RN 114522-16-6 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy- $\beta$ -D-erythropentofuranosyl)-3,6-dihydro- (CA INDEX NAME)

IT 676607-98-0P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(treatment of viral diseases 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof)

RN 676607-98-0 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-1-[2-deoxy-5-0-(1-oxohexadecyl)- $\beta$ -D-erythro-pentofuranosyl]-5,6-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L25 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Novel dosage form comprising modified-release and immediate-release active ingredients

AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.

AN 2006:100738 CAPLUS <<LOGINID::20080222>>

DN 144:198849

TI Novel dosage form comprising modified-release and immediate-release active ingredients

IN Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar

PA India

SO U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

r AIN.	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡΙ	US 2006024365 IN 2002MU00697	A1 A	20060202 20040529	US 2005-134633 IN 2002-MU697	20050519 < 20020805 <
	IN 193042 IN 2002MU00699 IN 2003MU00080	A1 A A	20040626 20040529 20050204	IN 2002-MU699 IN 2003-MU80	20020805 < 20030122
	IN 2003MU00082 US 2004096499	A A1	20050204	IN 2003-MU82 US 2003-630446	20030122 20030729 <
PRAI	IN 2002-MU697 IN 2002-MU699 IN 2003-MU80	A A A	20020805 20020805 20030122	<	
	IN 2003-MU82 US 2003-630446	A A2	20030122 20030729		

IT 62488-57-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (novel dosage form comprising modified-release and immediate-release active ingredients)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

L25 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Compounds, compositions and methods for modulating fat metabolism for treatment of metabolic disorders

AB Methods and compns. of identifying candidate compds., for modulating fat metabolism and/or inhibiting Apobec-1 activity are provided. The invention relates to compds. and pharmaceutical compns. which are useful for regulating fat metabolism and can be used for treatment of diseases and disorders selected from the group consisting of overweight, obesity, atherosclerosis, hypertension, non-insulin dependent diabetes mellitus, pancreatitis, hypercholesteremia, hypertriglyceridemia, hyperlipidemia.

AN 2004:368857 CAPLUS <<LOGINID::20080222>>

DN 140:386000

TI Compounds, compositions and methods for modulating fat metabolism for treatment of metabolic disorders

IN Gaudriault, Georges; Kilinc, Ahmet; Bousquet, Olivier; Goupil-Lamy, Anne;
Harosh, Itzik

PA Obetherapy Biotechnology, Fr.

SO PCT Int. Appl., 461 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

FAN.	PATE	-	10.			KIND DATE			APPLICATION NO.						DATE 			
PI	WO 2 WO 2					A2 A3		2004 2004		,	WO 2	003-	IL86	0		2	0031	023 <
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			GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KΖ,	LC,	LK,
			LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NΙ,	NO,	NZ,
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			KG,	KΖ,	MD,	RU,	ΤJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
			FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
			BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
	AU 2	20032	2746.	52	·	A1	•	2004	0513		AU 2	003-	2746	52	·	2	0031	023 <
PRAI	US 2	2002-	-420	316P		P		2002	1023	<-	_							

WO 2003-IL860 W 20031023

OS MARPAT 140:386000

IT 114522-16-6 686299-49-0D, stereoisomers

686299-50-3D, stereoisomers 686299-66-1D, stereoisomers

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(compds., compns. and methods for modulating fat metabolism for treatment of metabolic disorders)

RN 114522-16-6 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy- $\beta$ -D-erythropentofuranosyl)-3,6-dihydro- (CA INDEX NAME)

Absolute stereochemistry.

RN 686299-49-0 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1-pentofuranosyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 686299-50-3 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1-pentofuranosyl- (CA INDEX NAME)

RN 686299-66-1 CAPLUS

L25 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

 ${\tt TI}$  Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof  ${\tt GI}$ 

AB The invention discloses a genus of nucleoside or nucleotide analogs I [Y=C, CH, N; Z=C,CH,B; R1=H, acyl, NHNH2, etc; R2=absent, H, acyl, etc; R3=H, acyl, (un)substituted alkyl, etc.; R4, R4a=H, halo, OMe, OH; R5, R6=H, OR14 (R14= H, (un)substituted alkyl, etc.;) R7,R8=absent, H, acyl, etc.] for use as antiviral agents. In a first aspect, there is provided a compound according to Formula I as shown. In another aspect, the nucleoside and nucleotide analogs according to Formula I are used to treat a viral disease by administrating a therapeutically effective amount of a compound of Formula I to patient with a viral disease which is caused by an RNA virus, a DNA virus, a retrovirus, or HIV. Preparation of selected analogs is described.

AN 2004:290464 CAPLUS <<LOGINID::20080222>>

DN 140:297477

TI Treatment of viral diseases by 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof

IN Daifuku, Richard; Gall, Alexander; Sergueev, Dmitri

PA Koronis Pharmaceuticals, Incorporated, USA

SO PCT Int. Appl., 108 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

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PATENT NO.
                               DATE
                       KIND
                                          APPLICATION NO.
                                                                 DATE
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                               20040408
                                          WO 2003-US30200
                                                                 20030924 <--
РΤ
    WO 2004028454
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    WO 2004028454
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            GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
            LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
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            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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                               20040408 CA 2003-2499036
    CA 2499036
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                        A1
    AU 2003278904
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                               20050629
                                          EP 2003-770420
                         A2
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                         Τ
    JP 2006507255
                               20060302
                                        JP 2004-539890
                                                                 20030924 <--
PRAI US 2002-413337P
                         Ρ
                               20020924
    WO 2003-US30200
                         W
                               20030924
OS
    MARPAT 140:297477
ΙT
    114522-16-6P
    RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT
     (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
    USES (Uses)
        (treatment of viral diseases 1,3,5-triazine nucleoside and nucleotide
        analogs, and preparation thereof)
    114522-16-6 CAPLUS
RN
    1,3,5-Triazin-2(1H)-one, 4-amino-1-(2-deoxy-\beta-D-erythro-
CN
    pentofuranosyl)-3,6-dihydro- (CA INDEX NAME)
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Absolute stereochemistry.

IT 676607-98-0P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(treatment of viral diseases 1,3,5-triazine nucleoside and nucleotide analogs, and preparation thereof)

RN 676607-98-0 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-1-[2-deoxy-5-0-(1-oxohexadecyl)- $\beta$ -D-erythro-pentofuranosyl]-5,6-dihydro- (9CI) (CA INDEX NAME)

- L25 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Mutant p53-dependent growth suppression distinguishes PRIMA-1 from known anticancer drugs: A statistical analysis of information in the National Cancer Institute database
- AΒ We recently identified PRIMA-1 as a low mol. weight compound that restores tumor suppressor function to mutant p53 proteins and has anti-tumor activity in vivo (1). Here we report the statistical anal. of the effect of PRIMA-1 on a panel of human tumor cell lines using information available in a database at the Developmental Therapeutics Program of the National Cancer Institute (NCI). We extracted growth inhibition profiles for PRIMA-1 and 44 known anticancer agents, p53 status of cell lines, population doubling time, and level of p53 protein expression from the NCI database. The data were analyzed by linear regression, Wilcoxon matched pairs test, and cluster anal. In a subset of human cell lines derived from colon, ovarian, renal, and non-small cell lung cancer and melanoma, the level of mutant p53 expression correlated with cell population doubling time, r=-0.53, P=0.018. The GI50 values for PRIMA-1 correlated with levels of mutant p53, r=-0.75, P=0.0002. PRIMA-1 showed a statistically significant preference at P = 0.04 for growth inhibition of tumor cell lines expressing mutant p53 as compared with lines expressing wild-type p53. In contrast, none of several known anticancer drugs showed such preference. PRIMA-1 inhibited the growth of cell lines derived from various human tumor types in a mutant p53-dependent manner. This distinguishes PRIMA-1 from known anticancer drugs and supports the idea that PRIMA-1 can serve as a lead for the development of novel therapeutic compds.
- AN 2003:109003 CAPLUS <<LOGINID::20080222>>
- DN 139:46601
- TI Mutant p53-dependent growth suppression distinguishes PRIMA-1 from known anticancer drugs: A statistical analysis of information in the National Cancer Institute database
- AU Bykov, Vladimir J. N.; Issaeva, Natalia; Selivanova, Galina; Wiman, Klas G.
- CS Karolinska Institutet, Department of Oncology-Pathology, Cancer Center Karolinska (CCK), Stockholm, SE-171 76, Swed.
- SO Carcinogenesis (2002), 23(12), 2011-2018 CODEN: CRNGDP; ISSN: 0143-3334
- PB Oxford University Press
- DT Journal
- LA English
- IT 62488-57-7, 5,6-Dihydro-5-azacytidine
  RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);
  THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  (mutant p53-dependent growth suppression distinguishes PRIMA-1 from known anticancer drugs)
- RN 62488-57-7 CAPLUS
- CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 24

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ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 6 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
L25
    Combination therapy for reduction of toxicity of chemotherapeutic agents
ТΤ
AΒ
    Provided in the present invention are compds. suitable for treating
    neoplasms and tumors, viral, bacterial and parasite infections and
    combination therapy with these agents to lower the adverse side effects.
ΑN
    2002:695764 CAPLUS <<LOGINID::20080222>>
    137:210932
DN
    Combination therapy for reduction of toxicity of chemotherapeutic agents
ΤI
ΙN
    Prendergast, Patrick T.
PA
    Ire.
SO
    PCT Int. Appl., 66 pp.
    CODEN: PIXXD2
DT
    Patent
    English
LA
FAN.CNT 1
    PATENT NO.
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                                                                  DATE
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PΙ
    WO 2002069949
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                                                                  20020305 <--
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    WO 2002069949
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            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2002238799 20020919 AU 2002-238799 20020305 <--Α1 US 2002169140 US 2002-91855 Α1 20021114 20020306 <--PRAI IE 2001-209 20010306 <--Α WO 2002-IB632 W 20020305 <--

62488-57-7, 5,6-Dihydro-5-azacytidine ΙT

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy for reduction of toxicity of chemotherapeutic agents)

62488-57-7 CAPLUS RN

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

- L25 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- ΤI Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
- AΒ The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.
- ΑN 2002:521462 CAPLUS <<LOGINID::20080222>>
- 137:88442 DΝ
- TΙ Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
- ΙN Shanahan-Pendergast, Elisabeth
- PΑ Ire.
- SO PCT Int. Appl., 68 pp. CODEN: PIXXD2
- Patent DT
- English LA
- FAN.CNT 1

	PA:	CENT 1	NO.			KINI	D DA'	ΓE		APPL	ICAT	ION 1	NO.		D	ATE		
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	WO	2002	-IE1			W	20	020102	: <-	_								
OS	MAI	RPAT	137:	8844	2													
TT	62/	100_5	7_7															

- IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

- L25 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI DNA repair protein levels vis-a-vis anticancer drug resistance in the human tumor cell lines of the National Cancer Institute drug screening program
- AΒ Nucleotide excision repair (NER) is a multi-enzyme DNA repair pathway in eukaryotes. Several NER genes in this pathway including XPB, XPD, XPA and ERCC-1 have been implicated in anticancer drug resistance in human tumor cells. In this study, the authors assessed the levels of the above-mentioned proteins in the NCI panel of 60 human tumor cell lines in relation to the cytotoxicity patterns of 170 compds. that constitute the standard agent (SA) database. The database consists of drugs used in the clinic for which a mechanism of action has been at least partially defined. The ERCC-1, XPD and XPB protein expression patterns yielded significant neg. Pearson correlations with 13, 32 and 17 out of the 170compds., resp. (using). XPA produced a random assortment of neg. and pos. correlations, and did not appear to confer an overall resistance or sensitivity to these drugs. Protein expression was also compared with a pre-defined categorization of the standard agents into six mechanism-of-action groups resulting in an inverse association between XPD and alkylating agent sensitivity. The authors present data demonstrate that XPD protein levels correlate with resistance to alkylating agents in human tumor cell lines suggesting that XPD is implicated in the development of this resistance. NER activity, using the in vitro cell-free system repair assay, revealed no correlation between NER activity and the level of XPD protein in four cell lines with widely varying XPD protein levels. This lack of correlation may be due to the contribution of XPD to other functions including interactions with the Rad51 repair pathway.
- AN 2002:469230 CAPLUS <<LOGINID::20080222>>
- DN 138:32948
- TI DNA repair protein levels vis-a-vis anticancer drug resistance in the human tumor cell lines of the National Cancer Institute drug screening program
- AU Xu, Zhiyuan; Chen, Zhong-Ping; Malapetsa, Areti; Alaoui-Jamall, Moulay; Bergeron, Josee; Monks, Anne; Myers, Timothy G.; Mohr, Gerard; Sausville, Edward A.; Scudiero, Dominic A.; Aloyz, Raquel; Panasci, Lawrence C.
- CS Lady Davis Institute for Medical Research, Sir Mortimer B Davis-Jewish General Hospital, Montreal, QC, H3T 1E2, Can.
- SO Anti-Cancer Drugs (2002), 13(5), 511-519 CODEN: ANTDEV; ISSN: 0959-4973
- PB Lippincott Williams & Wilkins
- DT Journal
- LA English
- IT 62488-57-7, 5,6-Dihydro-5-azacytidine
  - RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (DNA repair protein levels vis-a-vis anticancer drug resistance in human tumor cell lines of National Cancer Institute drug screening

program)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Identification of active antiviral compounds against a New York isolate of West Nile virus

The recent West Nile virus (WNV) outbreak in the United States has AB increased the need to identify effective therapies for this disease. chemotherapeutic approach may be a reasonable strategy because the virus infection is typically not chronic and antiviral drugs have been identified to be effective in vitro against other flaviviruses. A panel of 34 substances was tested against infection of a recent New York isolate of WNV in Vero cells and active compds. were also evaluated in MA-104 cells. Some of these compds. were also evaluated in Vero cells against the 1937 Uganda isolate of the WNV. Six compds. were identified to be effective against virus-induced CPE with 50% effective concns. (EC50) less than 10  $\mu$ g/mL and with a selectivity index (SI) of greater than 10. Known inhibitors of orotidine monophosphate decarboxylase and inosine monophosphate dehydrogenase involved in the synthesis of GTP, UTP, and TTP were most effective. The compds. 6-azauridine, 6-azauridine triacetate, cyclopententylcytosine (CPE-C), mycophenolic acid and pyrazofurin appeared to have the greatest activities against the New York isolate, followed by 2-thio-6-azauridine. Anti-WNV activity of 6-azauridine was confirmed by virus yield reduction assay when the assay was performed 2 days after initial infection in Vero cells. The neutral red assay mean EC50 of ribavirin was only 106  $\mu g/mL$  with a mean SI of 9.4 against the New York isolate and only slightly more effective against the Uganda isolate. There were some differences in the drug sensitivities of the New York and Uganda isolates, but when comparisons were made by categorizing drugs according to their modes of action, similarities of activities between the two isolates were identified.

AN 2002:458415 CAPLUS <<LOGINID::20080222>>

DN 138:100377

TI Identification of active antiviral compounds against a New York isolate of West Nile virus

AU Morrey, John D.; Smee, Donald F.; Sidwell, Robert W.; Tseng, Christopher

CS Department of Animal, Dairy, and Veterinary Sciences, Institute for Antiviral Research, Utah State University, Logan, UT, 84322-4700, USA

SO Antiviral Research (2002), 55(1), 107-116 CODEN: ARSRDR; ISSN: 0166-3542

PB Elsevier Science B.V.

DT Journal

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LA English
IT 62488-57-7
   RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
            (identification of active antiviral compds. against a New York isolate
            of West Nile virus)
RN 62488-57-7 CAPLUS
CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1-β-D-ribofuranosyl-
      (CA INDEX NAME)
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Absolute stereochemistry.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI In vivo agents comprising antitumor cationic drugs, peptides, and metal chelators with acidic saccharides and glycosaminoglycans, giving improved site-selective localization, uptake mechanism, sensitivity and kinetic-spatial profiles

A drug carrier composition comprising a drug complexed with dermatan sulfate is AΒ disclosed. The drug is preferably an antitumor drug and may be taxol, a peptide oncoagent or vincristine. The most preferred antitumor drug is doxorubicin. The dermatan sulfate is essentially purified dermatan sulfate with a sulfur content of up to 9% (weight/weight) and with selective oligosaccharide oversulfation. The compns. are administered in a fashion that allows efficient vascular access and induces the following in vivo effects: 1) rapid, partial or total endothelial envelopment of the drug (diagnostic) carrier; 2) sequestration of the carrier and protection of the entrapped agent from blood vascular clearance at an early time (2 min) when the endothelial pocket which envelops the carrier still invaginates into the vascular compartment; 3) acceleration of the carrier's transport across and/or through the vascular endothelium or subendothelial structures into the tissue compartment (interstitium); and 4) improvement of the efficiency with which the drug migrates across the endothelium, or epi-endothelial or subendothelial barriers, such that a lower total drug dose is required to obtain the desired effect relative to that required for standard agents. Analogous tissue uptake is described for transepithelial migration into the lungs, bladder and bowel.

AN 2000:589895 CAPLUS <<LOGINID::20080222>>

DN 133:198574

TI In vivo agents comprising antitumor cationic drugs, peptides, and metal chelators with acidic saccharides and glycosaminoglycans, giving improved site-selective localization, uptake mechanism, sensitivity and kinetic-spatial profiles

IN Ranney, David F.

PA Access Pharmaceuticals, Inc., USA

SO U.S., 109 pp. CODEN: USXXAM

DT Patent LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
 US 6106866 US 1995-509338	A	20000822 19950731		19950731 <

IT 62488-57-7

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(antitumor cationic drugs, peptides, and metal chelators with acidic saccharides and glycosaminoglycans, having site-selective localization and uptake mechanism)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

# RE.CNT 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Pharmaceutical compositions for treatment of diseased tissues

AB A method to treat diseased tissue is provided where a cytotoxic compound is administered to a patient in need of treatment in combination with an immunostimulant. Diseased cells and/or infectious microbes/viruses are killed by the cytotoxic compound in the presence of the immunostimulant. The cell components including cellular contents and cell membrane fragments are presented by the immunostimulant to the host animal as antigens to stimulate the immune responses toward other diseased cells of the same type(s), that either remain in the vicinity or reside in distant tissues or organs. The cytotoxic mol. and immunostimulant are preferably applied locally at high concns., either sequentially or, preferably, simultaneously. For example, the composition can be administered directly to a target cancer. The composition can be prepared in various forms, such as a paste, a time release molded solid shape, a solution, a mixture with emulsifier, etc. Alternatively, the cytotoxic mol. and immunostimulant are applied in sequence.

AN 2000:475560 CAPLUS <<LOGINID::20080222>>

DN 133:109949

TI Pharmaceutical compositions for treatment of diseased tissues

IN Lee, Clarence C.; Lee, Feng-Min

PA USA

SO PCT Int. Appl., 26 pp. CODEN: PIXXD2

DT Patent

LA English FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	WO 2000040269	A2	20000713	WO 2000-US191	20000105 <
	WO 2000040269	A3	20001130		

W: AU, CA, CN, JP

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-114906P P 19990105 <--

IT 62488-57-7, DHAC

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(DHAC; pharmaceutical compns. for treatment of diseased tissues)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

L25 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Modulation of gene expression by combination therapy with antisense oligonucleotide and gene product protein effector

AB The invention relates to the modulation of gene expression. In particular, the invention relates to compns. comprising antisense oligonucleotides which inhibit expression of a gene in operable association with protein effectors of a product of that gene, and methods of using the same. In addition, the invention relates to the modulation of mammalian gene expression regulated by methylation.

AN 2000:277883 CAPLUS <<LOGINID::20080222>>

DN 132:318052

TI Modulation of gene expression by combination therapy with antisense oligonucleotide and gene product protein effector

IN Besterman, Jeffrey M.; Macleod, Alan Robert; Siders, William M.

PA Methylgene, Inc., Can.

SO PCT Int. Appl., 99 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PAT	ΓΕΝΤ	NO.			KIN	D	DATE			APPL	ICAT	ION I	.OV		D.	ATE	
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     EP 1243289
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     US 6953783
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     AU 2004200032
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                                             AU 2004-200032
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PRAI US 1998-104804P
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     AU 1999-65194
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     US 1999-420692
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     WO 1999-US24278
                                 19991019
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     62488-57-7, 5,6-Dihydro-5-azacytidine
ΙT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (antisense oligonucleotide and gene product protein effector for gene
        expression modulation)
RN
     62488-57-7 CAPLUS
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Absolute stereochemistry.

(CA INDEX NAME)

CN

# RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Use of neoangiogenesis markers for diagnosis and treatment of tumors

1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-

AB Neoangiogenesis markers (i.e. antibodies or receptors for e.g. vascular

endothelial growth factor, placenta growth factor, acidic or basic FGF, transforming growth factor  $\alpha$  or  $\beta$ , hepatocyte growth factor, insulin-like growth factor I, glycoprotein B61, protein LERK-1, flk-1 receptor, etc.) or partial sequences thereof and antiangiogenic compds. and factors such as paclitaxel, endostatin, fibronectin peptide, and fumagillin are conjugated with active agents such as chemotherapeutic agents, radiosensitizers, photosensitizers, antibodies, oligonucleotides, radioactive metal complexes, etc., which may be bound to carriers, for treatment of tumors. Likewise, neoangiogenesis markers may be conjugated to diagnostic agents such as MRI, radiog., ultrasound, or near-IR contrast agents for tumor diagnosis. Thus, N', N', N''', N'''-tetrakis(tertbutoxycarboxymethyl)-N''-(hydroxycarboxymethyl)diethylenetriamine was converted to its N-hydroxysuccinimide ester, coupled to a Thy-1 antibody, complexed with 186Re, and injected i.v. into rabbits for detection of implanted VX2 tumors by scintigraphy with a gamma camera. 132:262172 Use of neoangiogenesis markers for diagnosis and treatment of tumors Krause, Werner; Muschick, Peter

ΑN

DN

ΤI

ΙN

Schering Aktiengesellschaft, Germany PA

SO PCT Int. Appl., 27 pp. CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

RN

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		RW:	,		,		DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,
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(use of neoangiogenesis markers for diagnosis and treatment of tumors) 62488-57-7 CAPLUS

1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-CN (CA INDEX NAME)

- L25 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI 5,6-dihydro-5'-azacytidine (DHAC) affects estrogen sensitivity in estrogen-refractory human breast carcinoma cell lines
- There is little effective therapy for patients with hormone-refractory AB breast cancer. Hormone resistance is frequently due to the transcriptional inactivation of the estrogen receptor (ER) gene. We determined the effect of DHAC, a cytosine DNA methyltransferase (CMT) inhibitor, on the estrogen sensitivity in three human breast carcinoma cell lines with intermediate to low levels of estrogen receptor (ER) expression: MCF7 (adriamycin-sensitive), MCF7M/Adr (adriamycin-resistant), and MDA-435, and one ER+ cell line, ZR75-1. Cells maintained in culture were exposed to DHAC or vehicle continuously for 14 days, then exposed to estradiol or tamoxifen and counted on day 21. Exposure to DHAC did not affect estrogen sensitivity in ZR-75-1 and MCF7M/Adr cells. DHAC treatment of MCF7 and  $\mbox{MDA-435}$  cells resulted in significant (p<0.05) growth stimulation in response to estrogen at 10-6 M, and to growth modulation by tamoxifen at 10-5 to 10-7 M. These data suggest that DHAC can restore the estrogen sensitivity in ER-breast cancer. Thus, DHAC and other novel CMT inhibitors may have a clin. application in treating estrogen-refractory breast cancer patients by restoring the estrogen sensitivity and allowing these patients to respond again to conventional therapy with estrogen antagonists.
- AN 1999:396073 CAPLUS <<LOGINID::20080222>>
- DN 131:208754
- TI 5,6-dihydro-5'-azacytidine (DHAC) affects estrogen sensitivity in estrogen-refractory human breast carcinoma cell lines
- AU Izbicka, Elzbieta; Davidson, Karen K.; Lawrence, Richard A.; Macdonald, John R.; Von Hoff, Daniel D.
- CS Cancer Therapy and Research Center, The Nordan Colon Cancer Laboratory, Institute for Drug Development, San Antonio, TX, 78229, USA
- SO Anticancer Research (1999), 19(2A), 1293-1298 CODEN: ANTRD4; ISSN: 0250-7005
- PB International Institute of Anticancer Research
- DT Journal
- LA English
- IT 62488-57-7, 5,6-Dihydro-5-azacytidine RL: BAC (Biological activity or effector, except adverse);

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(DHAC affects estrogen sensitivity in estrogen-refractory human breast carcinoma cell lines)

- RN 62488-57-7 CAPLUS
- CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

## RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L25 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI 5,6 dihydro-5'-azacytidine (DHAC) restores androgen responsiveness in androgen-insensitive prostate cancer cells
- AB The androgen resistance of some prostate cancer patients may be due to transcriptional inactivation of the androgen receptor (AR) gene catalyzed by cytosine DNA methyltransferase. To determine if an inhibitor of cytosine DNA methyltransferase, 5,6-dihydro-5'-azacytidine (DHAC), can restore the androgen sensitivity in androgen-insensitive human prostate carcinoma cell lines in vitro, we cultured androgen-insensitive (PC3, DU-145, and TSUPrl) and androgen-responsive (LNCaP) cells with subcytotoxic concns. ( $\leq$ IC50) of DHAC for 14 days followed by exposure to dihydrotestosterone (DHT) or to hydroxyflutamide for 7 days. Only DHAC-treated DU-145 cells showed growth stimulation by 10-11 to 10-9 M DHT and a partial inhibition by 10-5 and 10-6 M hydroxyflutamide. However, since DU-145 is the only cell line tested that is known to have a hypermethylated AR promoter, the observed effects may be due to a partial demethylation of the AR by DHAC. Our data provide an evidence that cytosine DNA methyltransferase inhibitors can restore androgen responsiveness in androgen-refractory tumor cells, which are then sensitive to growth inhibition by antiandrogens.
- AN 1999:396072 CAPLUS <<LOGINID::20080222>>
- DN 131:223166
- TI 5,6 dihydro-5'-azacytidine (DHAC) restores androgen responsiveness in androgen-insensitive prostate cancer cells
- AU Izbicka, Elzbieta; Macdonald, John R.; Davidson, Karen; Lawrence, Richard A.; Gomez, Lionel; Von Hoff, Daniel D.
- CS Cancer Therapy and Research Center, Institute for Drug Development, San Antonio, TX, 78229, USA
- SO Anticancer Research (1999), 19(2A), 1285-1291 CODEN: ANTRD4; ISSN: 0250-7005
- PB International Institute of Anticancer Research
- DT Journal
- LA English
- IT 62488-57-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(DHAC restores androgen responsiveness in androgen-insensitive prostate cancer cells)

- RN 62488-57-7 CAPLUS
- CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

#### ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L25 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Dihydro-5-azacytidine and cisplatin in the treatment of malignant mesothelioma a phase II study by the cancer and leukemia group B
- AΒ In a prior Cancer and Leukemia Group B (CALGB) Phase II trial of patients with advanced, previously untreated mesothelioma, dihydro-5-azacytidine (DHAC) demonstrated a 17% response rate, including 1 complete response, with only mild myelosuppression. This Phase II study (CALGB 9031) was conducted to determine the effectiveness of and toxicities that would result from adding cisplatin to DHAC administered to the same patient population. Thirty-six patients were treated with concurrent DHAC at 1500 mg/m2/day for 5 days by continuous infusion and cisplatin 15 mg/m2 daily for 5 days. Therapy was repeated every 3 wk. Cisplatin was to be increased to 20 mg/m2 daily in subsequent cycles if toxicity was minimal. Therapy was continued until disease progression or excessive toxicity mandated discontinuation. Overall, 5 objective responses were observed in 29 evaluated patients (objective response rate, 17%). The median duration of response was 6.6 mo. Median survival was 6.4 mo, with a median time to  $\operatorname{clin}$ . failure of 2.7 mo. The major toxicity noted was significant chest/pericardial pain, as was observed with DHAC alone. There were 2 early deaths of unknown cause on Days 9 and 17 of therapy, resp. Significant leukopenia was observed in 29% of patients, but there were no neutropenic fevers. The addition of cisplatin to DHAC did not increase the response rate over that observed with DHAC alone in patients with mesothelioma; however, it did increase toxicity, especially leukopenia. This combination is not recommended for further studies involving mesothelioma patients.
- AN 1998:292263 CAPLUS <<LOGINID::20080222>>
- DN 129:23072
- TI Dihydro-5-azacytidine and cisplatin in the treatment of malignant mesothelioma a phase II study by the cancer and leukemia group B
- AU Samuels, Brian L.; Herndon, James E., II; Harmon, David C.; Carey, Robert; Aisner, Joseph; Corson, Joseph M.; Suzuki, Yasunosuke; Green, Mark R.; Vogelzang, Nicholas J.
- CS Lutheran General Hospital, Park Ridge, IL, USA
- SO Cancer (New York) (1998), 82(8), 1578-1584 CODEN: CANCAR; ISSN: 0008-543X
- PB John Wiley & Sons, Inc.
- DT Journal
- LA English
- IT 62488-57-7
  - RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (dihydro-5-azacytidine/cisplatin treatment of malignant mesothelioma in humans)
- RN 62488-57-7 CAPLUS
- CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

## RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L25 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Use of 5,6-dihydro-5-azacytidine in the treatment of prostate cancer
- AB A method for treating prostate cancer comprises administering an effective amount of 5,6-dihydro-5-azacytidine, or a pharmaceutically acceptable salt thereof, either alone or in combination with hormonal therapy. The invention includes a method for increasing expression of the androgen receptor in a prostate cancer cell, a method of increasing E-cadherin expression in a prostate cancer cell, and a method of inducing apoptosis in a prostate cell.
- AN 1998:87620 CAPLUS <<LOGINID::20080222>>
- DN 128:123806
- TI Use of 5,6-dihydro-5-azacytidine in the treatment of prostate cancer
- IN Von Hoff, Daniel D.; Izbicka, Elzbieta
- PA Ilex Oncology, Inc., USA
- SO PCT Int. Appl., 34 pp.
- CODEN: PIXXD2
  DT Patent
- LA English
- FAN.CNT 1

11114	PA:	CENT	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D.	ATE	
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			PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	UA,	UG,	UZ,
			VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ΤJ,	TM				
		RW:	GH,	ΚE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	DE,	DK,	ES,	FΙ,	FR,
			GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
			GN,	ML,	MR,	ΝE,	SN,	TD,	ΤG									
	ΑU	9740	461			A		1998	0210		AU 1	997-	4046	1		1	9970'	722 <
PRAI	US	1996	-220	42P		P		1996	0722	<-	_							
	WO	1997	-US1	3102		W		1997	0722	<-	_							
TТ	624	188-5	7-7.	5.6	-Dih	vdro.	-5-a	zacv	tidi	ne								

IT 62488-57-7, 5,6-Dihydro-5-azacytidine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dihydroazacytidine, alone or in combination, for prostate cancer treatment)

- RN 62488-57-7 CAPLUS
- CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

- L25 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
- TI Dihydro-5-azacytidine in malignant mesothelioma: a phase II trial demonstrating activity accompanied by cardiac toxicity
- AB Malignant mesothelioma is a disease that is refractory to chemo-therapy. Therefore, the objective of this multi-institutional, cooperative group Phase II trial was to determine the efficacy of dihydro-5-azacytidine (DHAC), a pyrimidine analog, in the treatment of malignant mesothelioma. Forty-one patients with histol. confirmed malignant mesothelioma received 120-h continuous infusions of DHAC (1500 mg/M2/day every 21 days) until maximal response, intolerable toxicity, or disease progression. One patient had a complete response, two had objective partial responses, and four had regression of evaluable disease. The overall response rate was 17%. one complete responder remains without disease progression at 6 yr. Chest pain and nausea were the most common toxicities. Supraventricular tachycardia and pericardial effusion occurred in 20% and 15% of patients, resp. In most patients, gastrointestinal effects were manageable. There was no significant hematol. toxicity. In malignant mesothelioma, a disease that is refractory to chemo-therapy, dihydro-5-azacytidine has definite antitumor activity. Its modest hematol. toxicity profile favors its use in combination with other agents. Caution regarding cardiac arrhythmias and pericardial effusion is necessary.
- AN 1997:368731 CAPLUS <<LOGINID::20080222>>
- DN 127:60299
- TI Dihydro-5-azacytidine in malignant mesothelioma: a phase II trial demonstrating activity accompanied by cardiac toxicity
- AU Vogelzang, Nicholas J.; Herndon, James E.; Cirrincione, Constance; Harmon, David C.; Antman, Karen H.; Corson, Joseph M.; Suzuki, Yasunosuke; Citron, Marc L.; Green, Mark R.
- CS Section of Hematology/Oncology, University of Chicago Medical Center, Chicago, IL, 60637-1470, USA
- SO Cancer (New York) (1997), 79(11), 2237-2242 CODEN: CANCAR; ISSN: 0008-543X
- PB Wiley
- DT Journal
- LA English
- IT 62488-57-7

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dihydro-5-azacytidine in malignant mesothelioma dealing with a phase II trial demonstrating activity accompanied by cardiac toxicity in humans)

- RN 62488-57-7 CAPLUS
- CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

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L25 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN
    Complexes of dermatan sulfate and drugs with improved pharmacokinetics
TΙ
AΒ
    A drug carrier composition comprising a drug complexed with dermatan sulfate
    (I), with a sulfur content of up to 9 %, is disclosed. The compns. are
    administered in a fashion that allows efficient vascular access and
    induced the following in vivo effects (1) rapid partial or total
    endothelial envelopment of the drug (diagnostic) carrier: (2)
    sequestration of the carrier and protection of the entrapped agent or
    blood vascular clearance at an early time (2 min) when the endothelial
    pocket which envelops the carrier still invaginates into the vascular
    compartment; (3) acceleration of the carrier's transport across and/or
    through the vascular endothelium or subendothelial structures into the
    tissue compartment (intestitium); and (4) improvement of the efficiency
    with which the drug migrates across the endothelium of epi-endothelial or
    subendothelial barriers, such that a lower total drug dose is required to
    obtain the desired effect relative to that required for standard agents.
    Analogous tissue uptake is described for transepithelial migration into
    the lungs, bladder and bowel. A solution of 10 mg I/mL was stirred with a
    solution of 4 mg doxorubicin (II)/mL and homogenized to obtain I:II complex.
    The solution was filtered , followed by addition of 3 mL of 500 \text{ mg/mL}
saccharose
    and 1.5 mL of 10 mg/mL PEG, the resulting solution was then filtered and
    lyophilized. The MIC50 of the complex against II-resistant human breast
    carcinoma cell was 0.81-0.89 as compared to 22.28~\mu\text{M} for II alone.
ΑN
    1996:529503 CAPLUS <<LOGINID::20080222>>
    125:177401
DN
ΤI
    Complexes of dermatan sulfate and drugs with improved pharmacokinetics
ΙN
    Ranney, David F.
PA
    Access Pharmaceuticals, Inc., USA
SO
    PCT Int. Appl., 227 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
FAN.CNT 1
    PATENT NO.
                  KIND DATE APPLICATION NO. DATE
                       ____
    WO 9619242
                        A1 19960627 WO 1994-US14776
PΙ
        W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,
            GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,
            NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN
        RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
            MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
            TD, TG
    CA 2208566
                               19960627
                                          CA 1994-2208566
                                                                  19941222 <--
                         Α1
    AU 9515537
                               19960710
                                          AU 1995-15537
                                                                  19941222 <--
                         Α
    AU 709008
                         В2
                               19990819
                                         EP 1995-907242
    EP 794796
                        Α1
                               19970917
                                                                  19941222 <--
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
                    T
    JP 10510831
                               19981020
                                         JP 1994-519745
                                                                  19941222 <--
PRAI WO 1994-US14776
                               19941222
                                        <--
    62488-57-7DP, reaction products with glycosaminoglycans
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (complexes of dermatan sulfate and drugs with improved
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RN 62488-57-7 CAPLUS

pharmacokinetics)

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

L25 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

Micronuclei induced by modulators of methylation: analogs of 5-azacytidine ТΤ AΒ Jones and coworkers demonstrated a qual. correlation between 5-azacytidine and some of its analogs in inducing changes in cell morphol. and their ability in preventing DNA methylation. Previously, we evaluated the same compds. to determine their ability to induce trifluorothymidine (TFT) resistance in L5178Y mouse cells and found that their mutagenic potency also correlated with their reported ability to induce morphol. changes in C3H10T1/2 cells. Here, we examined four of the same analogs, 5-fluoro-2'-deoxycytidine, 5-azacytidine, 5, 6-dihydro-5-azacytidine and 6-azacytidine, to find out if micronuclei induced by these compds. correlated with these effects. The most cytotoxic analog was 5-fluoro-2'-deoxycytidine, followed by 5-azacytidine. 5,6-Dihydro-5-azacytidine and 6-azacytidine were substantially less cytotoxic. All four compds. induced micronuclei. The lowest dose ranges at which responses were observed for micronucleus induction were .apprx.0.04  $\mu\text{M}$  for 5-fluoro-2'-deoxycytidine, 0.2  $\mu\text{M}$  for 5-azacytidine and 10-20  $\mu\text{M}$  for 5,6-dihydro-5-azacytidine and 6-azacytidine. Lack of kinetochore staining in most of the micronuclei indicated that all four compds. were clastogenic. We note a general trend in the biol. activity of these analogs: compds. that are specifically blocked at the 5 position such as 5-azacytidine and 5-fluoro-2'-deoxycytidine effect changes in cell morphol., cytotoxicity, TFT resistance and the induction of micronuclei at very low doses. 5-Azacytidine analogs that possess more chemical accessible 5 positions such as 5,6-dihydro-5-azacytidine and 6-azacytidine either require doses that are orders of magnitude greater to induce these effects or are unable to induce changes in cell morphol. and TFT resistance at doses below which the compound is lethal to the cells.

AN 1995:707279 CAPLUS <<LOGINID::20080222>>

DN 123:132224

TI Micronuclei induced by modulators of methylation: analogs of 5-azacytidine

AU Stopper, Helga; Koerber, Carsten; Gibis, Petra; Spencer, Diane L.; Caspary, William J.

CS Inst. Pharmacology and Toxicology, Univ. Wuerzburg, Wuerzburg, 97078, Germany

SO Carcinogenesis (1995), 16(7), 1647-50 CODEN: CRNGDP; ISSN: 0143-3334

PB Oxford University Press

DT Journal

LA English

IT 62488-57-7, 5,6-Dihydro-5-azacytidine RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (micronuclei induced by analogs of azacytidine and role of DNA methylation)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

L25 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI Biochemical pharmacology and DNA methylation studies of arabinosyl 5-azacytidine and 5,6-dihydro-5-azacytidine in two human leukemia cell lines PER-145 and PER-163

 $1-\beta-D-A$ rabinofuranosyl-5-azacytosine (ara-AC) and AB 5,6-dihydro-5-azacytidine (DHAC) are two new antitumor agents under clin. investigations, which exhibit the chemical similarities found in the tumoricidal drug cytosine arabinoside (ara-C) and the nitrogen substitution in the 5 position of the pyrimidine ring found in 5-azacytidine (5-aza-C). The cellular anabolism of ara-AC and DHAC and their effect on DNA methylation have been examined in two new human leukemia cell lines, which are sensitive (PER-145) and resistant (PER-163) to ara-C. The triphosphate anabolite of ara-AC, ara-ACTP, was the major cellular anabolite in the cellular exts. of the PER-145 cells, reaching a cellular saturation concentration of  $64.1~\mu\mathrm{M}$  using  $25~\mu\mathrm{M}$  of the drug. Only trace levels of ara-ACTP were detected in the PER-163 cell line, which lacks deoxycytidine kinase, after exposure to a similar concentration Notably, after 1 mM, the ara-ACTP concentration averaged 12  $\mu$ M. DHAC was anabolized by both cell lines to a similar degree but required much higher nucleoside concns. (100  $\mu$ M or higher) to achieve similar cellular concns. of its triphosphate, DHACTP. Although the deoxy derivative, DHAdCTP, was detected in both cell lines, it was detected at 1-2 log10 lower concns. than DHACTP. DNA methylation studies showed that DHAC had a profound effect in inducing DNA hypomethylation in both cell lines, with nadir values of 27.3 and 29.2% of control. Ara-AC induced 45% DNA hypomethylation in PER-145 cells, but did not alter the DNA methylation pattern in PER-163 cells, except when they were exposed to 1 mM of the drug for 24 h. These results could be explained by the differential biochem. activation of these drugs in the human leukemia cell lines.

AN 1995:550185 CAPLUS <<LOGINID::20080222>>

DN 123:25321

TI Biochemical pharmacology and DNA methylation studies of arabinosyl 5-azacytidine and 5, 6-dihydro-5-azacytidine in two human leukemia cell lines PER-145 and PER-163

AU Kees, Ursula R.; Avramis, Vassilios I.

CS Inst. Child Health Res., Princess Margaret Hosp., West Perth, Australia

SO Anti-Cancer Drugs (1995), 6(2), 303-10 CODEN: ANTDEV; ISSN: 0959-4973

PB Rapid Science Publishers

DT Journal

LA English

IT 62488-57-7, DHAC

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(biochem. pharmacol. and DNA methylation studies of arabinosyl azacytidine and dihydroazacytidine in sensitive and resistant human leukemia cells)

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

Absolute stereochemistry.

L25 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2008 ACS on STN

TI The synthesis, structure, and antitumor activity of 5,6-dihydro-5-azacytidine

GΙ

5,6-Dihydro-5-azacytidine (I) [62488-57-7], and nontoxic acid addition salts such as the hydrochloride [62402-31-7], are prepared from 5-azacytidine (5-AC) [320-67-2] by reduction of the 5,6-double bond of 5-AC with an alkali metal borohydride such as NaBH3. I showed an antitumor activity in murine leukemia systems L1210 and P388. In comparison with the parent compound, 5-AC, the antitumor activity was comparable, and I exhibited a more favorable therapeutic index. It also had better solution stability over a broad pH range.

AN 1977:462862 CAPLUS <<LOGINID::20080222>>

DN 87:62862

OREF 87:9926h,9927a

TI The synthesis, structure, and antitumor activity of 5,6-dihydro-5-azacytidine

IN Beisler, John A.; Abbasi, Mohamed M.; Driscoll, John S.

PA United States Dept. of Health, Education, and Welfare, USA

SO U. S. Pat. Appl., 17 pp. Avail. NTIS. CODEN: XAXXAV

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	US 712854	A0	19760808	US 1976-712854	19760808 <
PRAI	US 1976-712854		19760808	<	

IT 62402-31-7P 62488-57-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation and antitumor activity of)

RN 62402-31-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 62488-57-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-(CA INDEX NAME)

AB In mice, NSC-264,880 (dihydro-5-azacytidine-HCl)(I) [62402-31-7] had comparable activity to 5-azacytidine [320-67-2] against L1210 leukemia. I was inactive against a L1210 subline that was resistant to 5-azacytidine, indicating that I may be converted to 5-azacytidine in vivo. I was synthesized by reduction of the 5,6 double bond of 5-azacytidine followed by conversion to the HCl salt.

AN 1977:165237 CAPLUS <<LOGINID::20080222>>

Т

DN 86:165237

OREF 86:25889a,25892a

TI Dihydro-5-azacytidine hydrochloride, a biologically active and chemically stable analog of 5-azacytidine

AU Beisler, John A.; Abbasi, Mohamed M.; Driscoll, John S.

CS Natl. Cancer Inst., NIH, Bethesda, MD, USA

SO Cancer Treatment Reports (1976), 60(11), 1671-4 CODEN: CTRRDO; ISSN: 0361-5960

DT Journal

LA English

IT 62402-31-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as neoplasm inhibitor)

RN 62402-31-7 CAPLUS

CN 1,3,5-Triazin-2(1H)-one, 4-amino-3,6-dihydro-1- $\beta$ -D-ribofuranosyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl